



Assessment of Spirometry in Patients with Chronic Obstructive Pulmonary Disease and Its Correlation with High-Resolution Computerized Tomographic Scan Findings

S.Thiyagesa Deva Ganapathy¹, Udhayakumar.K² and R.Pajanivel^{3*}

¹Assistant professor, Sri Muthukumar Medical College and Research Institute, Chennai

²Associate Professor, Department of Radiodiagnosis, Mahatma Gandhi Medical college and research institute, Sri Balaji Vidyapeeth, Puducherry, India

³Prof and head., Department of Pulmonary Medicine, Mahatma Gandhi Medical college and research institute, Sri Balaji Vidyapeeth, Puducherry, India

Abstract: Chronic Obstructive Pulmonary Disease (COPD) is a chronic inflammatory lung disease characterized by persistent airway inflammation. Spirometry is considered a gold standard for diagnosing COPD severity, high Resolution CT is needed for the analysis of various phenotypes of COPD and to quantify emphysema. Therefore, we conducted a study for assessment of the clinical severity of COPD using spirometry and correlating it with the High-Resolution CT finding. The present study subjects were new and previously diagnosed COPD patients who were fulfilling the inclusion criteria were enrolled in the study. The total study population is 45 patients. All the Patients who are enrolled in the study were subjected to pulmonary function test assessment and they are subjected to High Resolution Computed Tomography and the severity is correlated. Among 45 patients enrolled in the study, the majority of the patients were in the age group of more than 61 years (71.1%). 13.3% of patients had mild COPD, 51.1 % moderate COPD, 26.7% severe and 8.8% very severe COPD patients with mean post-bronchodilator FEV1 (57.17) based on GOLD guidelines. In our study 44.4 % are smokers, 20 %are Ex-smokers and 35.6% are non-smokers. Out of the non-smokers, 10 were female and 6 were male patients (37.5%) and Smoking status is statistically significant in our study with a P value of 0.023. On correlating the High Resolution CT finding with the Spirometry, 35 patients had bronchial wall thickening, on comparing it with the COPD GOLD staging mild (33%), moderate (69%), severe (92%), very severe (100%). The p-value is 0.025. Emphysema was seen in 83%(n=5/6) of mild, 91% of moderate 75% of severe, and 100% of very severe patients and it correlated well with Spirometry and the p-value is 0.005, Mean lung density decreased with a decrease in Post FEV1%. The severity of emphysema and Bronchial wall thickening correlated well with the High-Resolution CT finding and they showed a positive correlation with Post FEV1.

Keywords: COPD, Spirometry, CT Scan, Chronic Obstructive and Correlation

*Corresponding Author

R.Pajanivel, Professor and head, Department of Ophthalmology, Mahatma Gandhi medical college, Sri Balaji Vidyapeeth, Pondicherry, India

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1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD), is the fourth leading cause of death in the world¹, represents an important public health challenge that is both preventable and treatable. Globally, the COPD burden is projected to increase in the coming decades because of continued exposure to COPD risk factors and the aging of the population. In the prevalence of mortality 3 out of 5 patients in India have a noncommunicable disease, in which COPD is the second largest cause.² INSEARCH study (Indian study on the epidemiology of asthma, respiratory symptoms, and chronic bronchitis in adults) showed the prevalence of COPD in India is 3.49 % and it is 4.46 % in males and 2.86 % in females. COPD prevalence has a wide range of variability of 1.1 % in Mumbai and 11% in Thiruvananthapuram.³ Chronic obstructive pulmonary disease includes emphysema of varying morphologic appearance, large airway abnormality, and small airway obstruction. Increasing awareness of the heterogeneity of COPD has led to increased use of CT to characterize COPD. Bullous lung disease can be better assessed by High resolution computed tomography (HRCT) thorax which helps in the early identification and prediction of recurrence of Secondary spontaneous pneumothorax and complications of COPD like PAH can be identified in the early stage by HRCT which helps in early management. Chronic obstructive pulmonary disease (COPD) has considerable diversity in its clinical manifestations and rate of progression of the disease among affected individuals, owing to differences in pulmonary morphologic abnormalities, at least in part. Customarily, symptom assessment, spirometric assessment, and the frequency of respiratory exacerbations were used to determine symptom severity and assist management. Chest computed tomography (CT) is a noninvasive imaging method that offers ample insight into structural and pathophysiologic pulmonary variables, allowing for a better knowledge of disease variability and further phenotyping of COPD. Over time, many new physiologic methods were invented to identify these early small airway variations in smokers prior to the emergence of overt COPD, as explained by the FER. However, none were robust or useful enough at the time of technological improvement to be used in a clinical laboratory or medical office. Such efforts continue, with increasing sophistication, but the FER remains the gold standard. The purpose of this study is to present current knowledge regarding the use of Quantitative CT for the assessment of mosaic attenuation, emphysema, bullae, bronchiectasis, fibrosis, pulmonary hypertension, bronchial wall thickening and correlating that with clinical grading of COPD using pulmonary function testing with GOLD guidelines.

2. METHODOLOGY

This study was an institutional cross-sectional study done in the department of Pulmonary Medicine at Mahatma Gandhi Medical College and Research Institute, Puducherry. This

study was approved by Institutional Human Ethical Committee of MGMCRI. The research work was done in accordance of declaration of Helsinki. All patients consented for the study. All the newly diagnosed COPD and previously diagnosed COPD patients attending the Pulmonary Medicine department who were willing for the study were enrolled in the study. The study population was 45 patients. After obtaining the written informed consent and explaining the procedure in the patient's language, patients with acute exacerbation of COPD, who cannot perform spirometry and are not willing to participate were excluded from the study.

2.1 Inclusion Criteria

Patient with symptoms of COPD and spirometry showing Post BD FEV1/FVC less than 70%, Known case of COPD on treatment

2.2 Exclusion Criteria

A patient presenting with acute exacerbation of COPD, recently diagnosed ischemic heart disease, smear-positive pulmonary tuberculosis, pregnant patients, hemoptysis, Pneumothorax., Recent thoracic or abdominal surgery, or Patients who are not giving consent for the procedure.

2.3 Study Protocol

A lung function test was done and categorized according to GOLD guidelines. COPD was confirmed and subjected to an HRCT scan and the following was noted. bronchial wall thickening mosaic attenuation, emphysema bullae, bronchiectasis, tracheal index fibrosis, and pulmonary hypertension were noted.

3. STATISTICS ANALYSIS

A simple convenient sample of consented patients was taken for the study. Still for the alpha value of 5 % and beta value of 80 % with an expected correlation value of 0.4, a sample size of 45 is adequate. All data were transported to EXCEL sheet and then SPSS software 20 USA and analyzed with multiple correlation analyses.

4. RESULTS

4.1 Demographic Data

Out of 45 patients based on the age distribution, the majority of the population were above 61 years of age (71.1%) and 28.9% were less than 60 years of age. Gender distribution 77.8% were males and 22.2% were females. Out of 45 patients 17.7%(n=8) of population are under BMI < 18.50 , 35.5%(n=16) were between 18.50 – 22.9 , 26.6%(n=12) were between 23-24.9 , 17.7%(n=8) were between 25-29.1 and 2.5%(n=1) were > 30 .

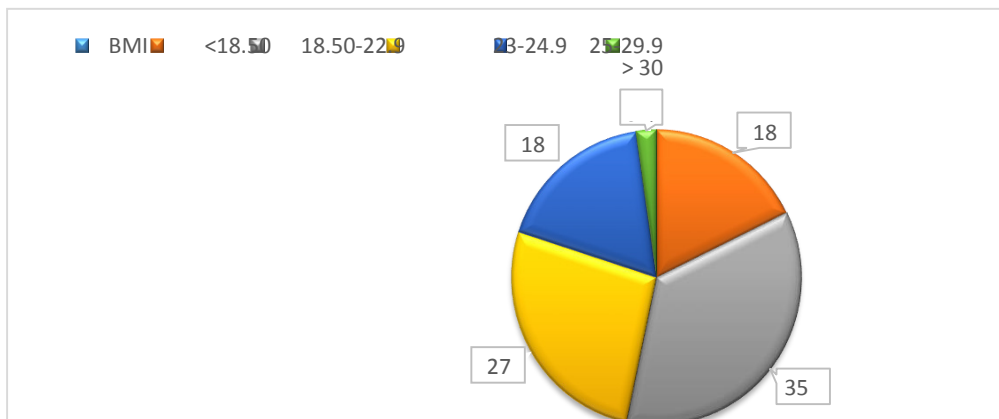


Fig 1 showing BMI of patients

Based on the smoking status 44.4%(n=20) patients were smokers, 20%(n=9) patients were Ex – Smoker, 35.6% (n=16) patients were non-smokers out of which 13.4%(n=6) were male and 22.2%(n=10) were female. Distribution of smoker in phenotypes of emphysema; in centriacinar emphysema 64.7 %

(n= 11) are smokers and 29.4 % (n=5) were Ex-Smokers. In panacinar emphysema 38.8 % (n=7) were smokers and 11.1 % (n=2) were Ex-Smokers. In paraseptal emphysema 1 patient was ex- smoker.

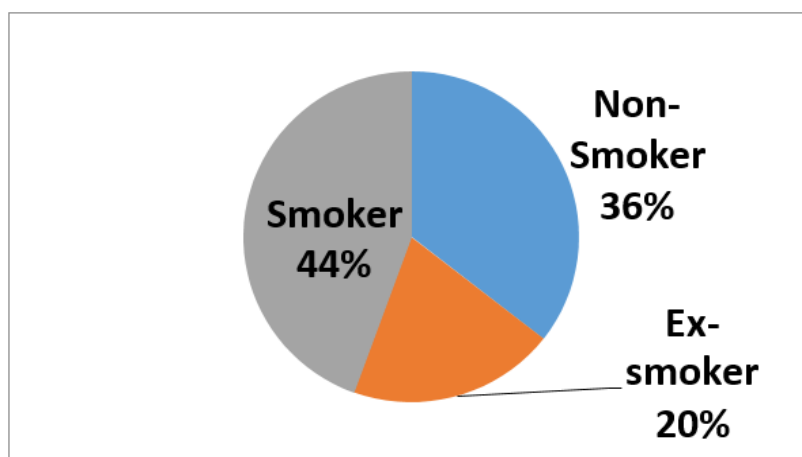


Fig 2 showing percentage of smokers, non-smokers and ex-smokers

4.2 Severity of Chronic Obstructive Pulmonary Disease Based On Spirometric and Its Distribution in Hrct Thorax

Based on the severity, on the basis of GOLD guidelines there are mild 13.3%(n=6), moderate 51.1 % (n=23) , Severe 26.7%(n=12) ,Very severe 8.9%(n=4) cases.

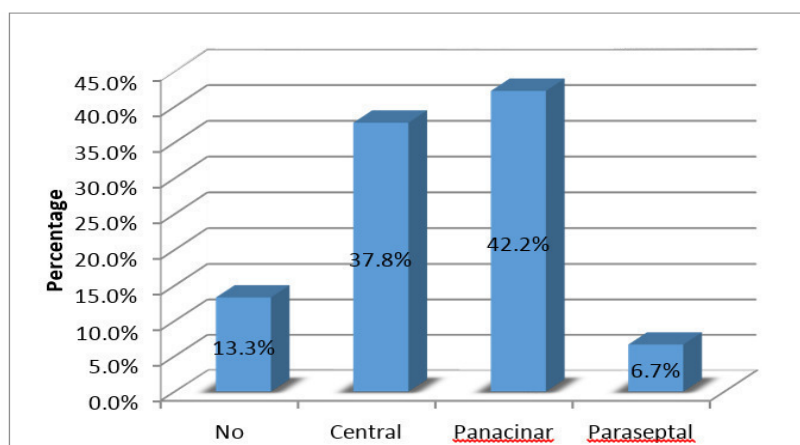


Fig 3 showing severity by GOLD guidelines

Based on the distribution of the pattern of emphysema, centriacinar emphysema was seen in 37.8%(n=17) of the population, panacinar emphysema in 42.2%(n=19), paraseptal emphysema in 6.7% (n=3) and 13.3%(n=6) population in the study had no emphysema. In our study, among 45 patients mosaic attenuation was seen in 11.1 % (n=5), and 22.2% of patients had bulla. Bronchial wall thickening is seen in 35(77.7%) patients and based on spirometry they are distributed as follows 33%(n=2) patients in mild, 78%(n=18) in moderate, 91.6%(n=11) in severe, and 100%(n=4) in the very severe group. In our study among 45 patients. Bronchiectasis was seen in 35.6% (n=16), 35.6 % (n=16) had fibrosis, 6.7 % (n=3) patients had pulmonary artery hypertension.

4.3 Correlation of HRCT Findings with Spirometric Severity

On correlating the smoking status and severity of COPD Smokers were distributed as 1 patient in the mild group, 6 in moderate group, 9 in severe group and 4 in very severe group. In Very severe group, all the patients were smokers. Non-smokers were predominantly seen in moderate group. Correlation between the severity of COPD with smoking status was statistically significant p value = 0.023

Table I showing Correlation analyses of COPD -GOLD stages and smoking					
SMOKING STATUS	COPD GOLD STAGE				P VALUE
	MILD	MODERATE	SEVERE	VERY SEVERE	
SMOKER	1	6	9	4	0.023
EX-SMOKER	2	6	1	0	
NON-SMOKER	3	11	2	0	

Among 45 patients, Emphysema was present in 86.66% and they were distributed as 11.1%(n=5) mild, 46.6%(n=21) moderate, 20%(n=9) severe and 100%(n=4) in very severe group, on correlating it with the FEV1 % it showed statistical significance with p value = 0.005

Table 2 showing the prevalence of emphysema in severity of COPD			
COPD GOLD STAGE	EMPHYSEMA		P value
	YES	NO	
Mild	5	1	0.005
Moderate	21	2	
Severe	9	3	
Very Severe	4	0	

Bronchial wall thickening was seen in 77.7 %(n=35/45) of the study population and they were distributed as follows 33%(n=2) in mild, 69%(n=18) in moderate, 92%(n=11) in severe cases and 100 %(n=4) in very severe patients. The correlation between the spirometry severity with the bronchial wall thickening was statistically significant with the p value = 0.025.

Table 3 showing the severity of bronchial wall thickening					
COPD GOLD STAGE	BRONCHIAL WALL THICKENING				P VALUE
	YES		NO		
MILD	2	33%	4	67%	0.025
MODERATE	18	69%	5	19%	
SEVERE	11	92%	1	8%	
VERY SEVERE	4	100%	0	0%	

The mean lung density was calculated in the coronal and sagittal section in both the right and left lung in the upper lobe and lower lobes and they were correlated with the spirometric severity. Coronal right upper lobe had P value =0.016, Coronal right lower lobe had p value = 0.02, Coronal left upper lobe p value =< 0.0001 and coronal left lower lobe p value = < 0.0001, Sagittal right upper lobe have P value =

<0.0001, Sagittal right lower lobe have P value =<0.0001, Sagittal left upper lobe have p value = 0.026 and Sagittal left lower lobe have P value= <0.0001. Among 45 patients the Pearson correlation was calculated for the mean lung density and the FEV1 percentage and the MLD had moderate positive correlation and statistically significant.

Table 4 showing complete correlation analyses								
FEV1%	CR_UL	CR_LL	CL_UL	CL_LL	SR_UL	SR_LL	SL_UL	SL_LL
PEARSON CORRELATION	0.441	0.318	0.582	0.516	0.438	0.455	0.367	0.624
SIG.(2-tailed)	.002	.033	<0.0001	<0.0001	.003	.001	.013	<0.0001

5. DISCUSSION

Out of 45 patients, most patients are between 60 and 70 years old. In our study, 71.1% were above the age of 61 years and 28.9% were below the age of 60 years. The calculated average age of the patient in this study was 65.3 years and the average age of male and female patients in this study were 66.28 years and 62.1 years respectively. A study done by Shrestha et al and Bhandari et al also had similar findings.⁴ Tobacco smoking is the most common risk factor for COPD and in the Indian population. Beedi smoking is more common (rural areas) compared to cigarette smoking. In our study there was statistical significance between association of smoking and COPD (P value = 0.023). A study done by Rafel et al showed that lifetime smokers have a 50% chance of developing COPD and smoking cessation can decrease the risk of getting COPD.⁵ In a study done by Elena et al states that the prevalence of current smoking is 26.5%, males (27%) and women (31%). The ex-smoker population represents 68.9%, while non-smokers comprise 1.5%. In her study 73% of male smokers have a moderate to severe COPD degree. She concluded that smoking is a major cause of COPD exacerbation and smoking is an important risk factor for COPD. A meta-analysis done by Kamal et al on reviewing 42 articles state that over 80% of COPD patients are smokers. He also states that persons with a pack year of more than 20 have a high 3-fold increase in chance of getting COPD.⁶

5.1 COPD and HRCT

There are two ways of assessing emphysema, they are quantitative and qualitative assessment. Quantitative assessment is by measuring the LAA (Low Attenuation Areas) and Qualitative assessment is based on visual assessment of emphysematous segments. In our study we assessed COPD based on qualitative and quantitative method. We also studied features like Bronchial wall thickening, Emphysema, Bullae, Mosaic attenuation, Bronchiectasis, Fibrosis and Pulmonary artery hypertension. For Quantitative analysis we calculated lung density (HU) in right upper lobe and lower lobe and left upper lobe and lower lobe, both in coronal and sagittal section. A study done by Umang shah et al in Mumbai studying 50 COPD patients and three predominant phenotypes were assessed like Emphysema, Bronchiectasis and Bronchial wall thickening. In his study out of 50 COPD patients 40 had Emphysematous changes (80%) and Bronchiectasis associated with COPD are 36% and Bronchial wall thickening seen in 72% of study population. Presence of Emphysema and Bronchiectasis, Bronchial wall thickening correlate with our study.⁷

5.2 Spirometry and HRCT Correlation

In our study out of 45 patients 35 patients had bronchial wall thickening. The distribution of Bronchial wall thickening based on COPD GOLD staging are mild (33%)n=2, moderate (69%)n=18, severe (92%)n=11, very severe (100%) n=4. The p value is 0.025. Bronchial wall thickening is suggestive of chronic bronchitis phenotype of COPD. Bronchial wall thickening will produce airflow limitation, leading to chronic bronchitis and increased mucus producing cells proliferation in the bronchial wall which in turn will lead to increased mucus production and cough with expectoration. In a study done by Onno et al in lung cancer screening patients, he studied 1140 male patients and assessed for CT biomarkers of COPD like Emphysema, air trapping and Bronchial wall thickness and he concluded that

the Sensitivity and specificity of all three parameters are 73.2% and specificity was 88%, the positive and negative predictive value are 80.2% and 84.2%.⁸ On correlating the HRCT finding and Emphysema, In our study, out of 45 patients 83%(n=5/6) of mild patients, 91%(n=21/23) of moderate patients, 75%(9/12) of severe patients, 100%(4/4) of very severe patients had emphysema and it had correlated well with the severity of COPD based on spirometry (P value = 0.005). Based on the type of emphysema 37.8%(n=17/45) had centriacinar pattern, 42.2%(n=19/45) had panacinar pattern, 6.7%(3/45) had paraseptal distribution and 13%(13.3%) had no emphysema. In a study done by Umang shah et al, the distribution of emphysema was 32% centriacinar emphysema, 22% panacinar emphysema, 26% paraseptal emphysema, and any type of emphysema seen in 20% of population. In our study patient with panacinar emphysema had predominant distribution among the population. Individuals with centriacinar predominant emphysema had significant smoking history and increased breathlessness on exertion compared with other phenotype, and they had increased low attenuation area (>-910HU) in HRCT thorax. The average normal attenuation of lung parenchyma is -800 HU. In our study we have calculated lung density less than -910 HU is considered as Emphysema. There are various studies which have assessed the significance of determining the threshold for the low attenuation area. In a study done by Wang et al the threshold of -925 to -965 HU had significant correlation with emphysema. He suggested that -950 HU threshold is significant for identifying emphysema.⁹ A study done by Muller et al used -910HU as threshold for the analysis of emphysema and it had significant correlation with visual assessment of emphysema. With the low threshold value mild cases of COPD can also be assessed significantly and early changes can be identified. In our study the low attenuation areas were assessed in the coronal and axial section of the right upper lobe, lower lobe and left upper lobe and lower lobe areas. The Mean lung density in our study was -952.49HU. The Lung density calculated for each lobe and the mean lung density for the coronal right upper lobe was -955.793. The mean lung density for coronal left upper lobe is -938.258, the mean lung density for coronal right lower lobe was -953.858, the mean lung density for coronal left lower lobe was -953.423, the mean lung density for sagittal right upper lobe was -951.858, the mean lung density for sagittal left upper lobe is -951.59, the mean lung density for sagittal right lower lobe was -956.589 and the mean lung density for sagittal left lower lobe was -958.585. In a study done by Young Kyung Lee et al, 82 patients were enrolled and clinical, radiological, HRCT findings were assessed and correlated.¹⁰ He concluded that HRCT findings like mean lung density correlated well with the pulmonary function testing and assessing both the airway thickness and mean lung density give precise data on emphysema. In his study, he had positive correlation with the mean lung density and FEV1 % $r = 0.439$ and the p value of 0.009. In our study comparing the Mean lung density (Low attenuation areas) and the FEV1 % showed positive correlation, when the post bronchodilator FEV1 decreases the lung density is also decreased (increased emphysema). In our study we calculated Pearson correlation for coronal section and sagittal section of both the upper lobe and lower lobes. They are CR_UL = 0.441, CR_LL = 0.318, CL_UL = 0.582, CL_LL = 0.516, SR_UL = 0.438, SR_LL = 0.455, SL_UL = 0.367, SL_LL = 0.624. The lobes showed positive correlation and the P value calculated showed all were statistically significant. Bulla is defined radiologically as a rounded focal lucency or area of decreased attenuation, 1 cm or more in diameter, bounded by a thin wall. In a study done

by Anubhith Singh et al he concluded that bullae is a common co existing feature of emphysema and Bullae were detected in 10 (28.57%) patients. Similar finding seen in Umang shah et al showed 22%(n=11) 50 patients had co existing bulla with emphysema. In our study, out of 45 patients 35.6 %(n=16) patients had bronchiectasis and 22% patients had both COPD and bronchiectasis co existing. Presence of bronchiectasis will increase the chance of infective exacerbation in COPD patients. Tracheal index was calculated in the study by high resolution CT .It is defined as ratio of transverse and antero posterior diameter 1 cm above the level of aortic arch. Saber sheath trachea is defined when the ratio is $<2/3$ or <0.67 . In our study only two patients had saber sheath trachea which is a sign of hyperinflation. Pulmonary artery hypertension seen in 6.7 %(n=3), Diagnosis of PAH in stable COPD is critical because cardiac work up is not done routinely and it is important to evaluate as presence of PAH since it affects the prognosis and exercise capacity even in stable COPD patients. There is no statistical correlation with severity of COPD in our study. In our study out of 45 patients 35.6% (n=16) had fibrotic changes in high resolution CT and there was no significant correlation with the progression of disease (p value = 0.101). In our study out of 45 patients 11.1 % (n=5) of patients had mosaic attenuation suggestive of small airway disease. There is no significant correlation between spirometry and mosaic attenuation pattern (P value = 0.267), as the Spirometry cannot precisely assess the Small airway disease. In comparison to Smoking -COPD, NonSmoking -COPD is seen in young adults, with an equal male-female predominance, and is primarily a small-airway illness with a phenotype but with much less emphysema, maintained lung diffusion, and a slower rate of worsening of pulmonary function⁷. According to Shah et al, ⁸the majority of nonsmokers are female, and smokers have a higher grade of dyspnea, more severe COPD, a lower post-bronchodilator FEV1, and more emphysematous changes on x-rays. Sousa et al suggested that CT phenotyping may help predicting ventilatory response to exercise in subjects with COPD¹⁰ have correlated with phenotypes and microbiology of patients with

COPD and hence such typing with CT scan is needed as suggested by our work

6. CONCLUSION

Based on the results and the methodology employed, we have concluded that Chronic obstructive pulmonary disease is a multi-phenotypic disease and pulmonary function test alone is not sufficient for the phenotyping. High Resolution Computed Tomography is warranted in all the COPD patients for diagnosing, phenotyping and assessing the prognosis of the condition. Quantification of Emphysema can be done by high-resolution CT and it correlates well with Spirometry severity of chronic obstructive pulmonary disease. Presence of bullous disease can be identified in High resolution CT which can impact the treatment plan for the patient. Surgical management is needed for the Bullous disease to prevent Secondary spontaneous pneumothorax (COPD is the most common cause of secondary spontaneous pneumothorax) and recurrence can be predicted. Emphysema, bronchial wall thickening and smoking status were statistically significant when correlating with spirometry severity of chronic obstructive pulmonary disease. COPD has various comorbid conditions like Pulmonary Artery Hypertension which can be assessed by High Resolution CT, Early identification of small airway disease and Prognosis can be assessed. Hence holistic evaluation of the disease condition is needed for the diagnosis and management, which can be done better by Quantitative High resolution CT compared with Pulmonary function test.

7. AUTHORS CONTRIBUTION

Dr TDG and UK have done the data collection while RP has done the write up and communication.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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